and for claim 65 at page 36, lines 25-35, page 37, lines 30-36 and page 38, lines 1-19. Reconsideration of the application as amended is respectfully requested.

OBJECTION TO CLAIM 57

Claim 57 stand objected to because the Examiner contends that as applicant is claiming a recombinant expression vector, applicant should specify that the nucleic acid sequence is linked to an expression control sequence. To facilitate prosecution, applicants have amended claim 57 to recite that the nucleic acid sequence is linked to an expression control element. Therefore, withdrawal of this objection is respectfully requested.

REJECTION OF CLAIMS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1-5 and 56-57 stand rejected under 35 U.S.C. §112, first paragraph because the Examiner contends that it would take undue experimentation to make and use the invention as claimed. Specifically, the Examiner contends, that "while being enabling for cDNA sequence of MART-1, (specifically SEQ ID NO:1) and gp100, it does not reasonably provide enablement for chromosomes, allelic variations, homologs or mutants thereof." Applicants traverse this rejection for the reasons presented below.

Contrary to the Examiner's contentions, the specification teaches what is meant by allelic variations (page 9, lines 20-35), homologs (page 17, lines 12-30), and what alterations may be present in the instantly claimed nucleic acid sequences (page 16, lines 24-30). Moreover, applicants teach how homologs or allelic variations may be obtained (page 17, lines 12-30), how to generate probes for isolating allelic variations or homologs (page

13, lines 26-32; page 14, lines 31-36; page 15, lines 1-35; page 16, lines 1-23; page 18, lines 10-28), and teaches hybridization conditions (page 46, lines 30-36 and page 47, lines 1-31) that may be used.

Applicants respectfully submit that an artisan having ordinary skill in the pertinent art could obtain the instantly claimed nucleic acid sequences with substantially no experimentation or with not an undue amount of experimentation. The instant disclosure provides sufficient information with respect to the nature and characteristics of the MART-1 nucleic acid sequence and amino acid sequence so that an artisan would know how to isolate homologs or alleles. There is no reason to believe that this nucleic acid sequence could not be utilized to obtain allele variations or homologs.

Moreover, it is impermissible to limit applicant to the working examples. The Examiner has failed to carry his burden since the Office Action has not provided any evidentiary basis for limiting the claims to the specifically presented embodiments. Applicants do not need to exemplify every possible claimed embodiment. In re Robins, 429 F.2d 452, 456-57, 166 USPQ 556, 575 (CCPA 1970). Applicants respectfully request withdrawal of the objection to the specification and rejection of the claims.

With respect to claim 56, applicants believe that this claim is fully enabled by the specification. Contrary to the Examiner's assertion, applicants urge that claim 56 defines a particular class of substances all of which are supported by the disclosure. Furthermore, the "comprising" terminology is believed to be proper. The number of peptides encompassed by the claim is delineated by three requirements. First, the nucleic acid sequences encoding the peptide must be derived or obtained from the MART-1 or gp-100 sequences; second, the

amino acids must be at least eight contiguous amino acids; and third, the peptides must be recognized by tumor infiltrating lymphocytes (TILs). Moreover, applicants specification provides assays by which to test such peptides (page 41, lines 6-35; page 42, lines 1-23; Example 2, page 56-65; and Example 3, page 74, lines 25-35, pages 75-76). Thus, the peptides do have specific function in that they must be recognized by TIL. Hence, it is submitted that the peptides defined in claim 56 are supported by the disclosure and the "comprising" terminology would not open the claim to materials as alleged by the Examiner. Applicants respectfully request withdrawal of this ground of rejection.

REJECTION OF CLAIMS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-5 and 56-57 stand rejected under 35 U.S.C. §112, second paragraph, for failing to distinctly point out and claim what applicants regard as the invention. Applicants traverse the rejection for the reasons stated below.

The inadvertent typographical errors in claim 56, line 5, and claim 57, line 1 have been deleted. For clarity and to facilitate prosecution, the language in claim 56, line 6 "being reactive to" has been amended to recite --recognized by--. For clarity, the full title of MART-1 has been inserted in the claims.

The Examiner contended claims 3-5 were vague and indefinite because the homologs, allelic variations, homologs or variants had not been defined. Cancellation of claims 1-5 render the Examiner's rejection moot with respect to those claims. In any event, for the reasons stated hereinabove for the 35 U.S.C. §112, first paragraph rejections,

applicants believes that the skilled artisan would understand the terminology used in these claims.

The Examiner also contends that the terminology "derived from" in claim 56 is "vague and indefinite". Applicants traverse this rejection.

Applicants submit that one of skill in the art would have known what is meant by the term "derived from." Moreover, applicants clearly disclose what is meant by "derived from" and provide examples of peptides "derived from" the sequences (page 8, lines 12-20; see page 35, lines 19-35; page 37, lines 30-36, page 38, lines 1-20). Given the instant disclosure the skilled artisan would be fully appraised of what "derived from" means. Withdrawal of this ground of this rejection is respectfully requested.

REJECTION OF CLAIMS UNDER 35 U.S.C. §102

Claim 1 stands rejected under 35 U.S.C. §102(a) as being anticipated by Maresh et al. DNA and Cell Biology, vol. 13(2), p.87 (2/94) or Gaugler et al. J. Exp. Medicine, vol. 179, p. 921. Claim 1 is also rejected under 35 U.S.C. 102(b) as being anticipated by Traversari et al. J. Exp. Med. vol. 176 p. 1453 (1992). Applicants traverse both these rejections for the reasons presented below.

The present invention relates to novel nucleic acid sequences which encode a melanoma antigen recognized by T-cells, which has been designated MART-1. The MART-1 melanoma antigen showed no significant homology to any known melanoma antigen (see

specification page 8, lines 33-35, page 9, lines 10-12). For a reference to be an anticipation it must recite each and every element of the claimed invention.

Maresh et al. describes a cDNA that involves a melanoma associated ME2O antigen. The cDNA for the ME20 antigen encodes gp100 (see page 37, lines 5-30) and thus represents a distinct and separate gene from the instantly claimed MART-1 nucleic acid sequence. As a distinct gene, encoding a protein distinct from MART-1, the ME20 cDNA cannot anticipate the instantly claimed sequences. Likewise, Gaugler et al. describes nucleic acid sequence encoding the MAGE-3 and MAGE-1 proteins. MAGE-1 and MAGE-3 also represent distinct genes and a distinct gene family from that of MART-1. Hence, they cannot anticipate the instantly claimed invention. Withdrawal of the 35 U.S.C. §102 rejection is respectfully requested.

Traversari et al. relates to a nonapeptide encoded by MAGE-1. MAGE-1 is encoded by a separate and distinct gene from MART-1, and is a member of the MAGE family of genes. Therefore, MAGE-1 nucleic acid sequences cannot anticipate the claimed invention. Withdrawal of the 35 U.S.C. §102 rejection is respectfully requested.

Claims 1 and 56-57 stand rejected under 35 U.S.C. §102(a) as being anticipated by Adema et al. Am. J. Pathol., vol. 143, p. 1579 (12/93). Claims 1 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Kwon et al. PNAS vol. 88 p. 9228 (1991). Applicants traverse both these rejections for the reasons presented below.

Adema et al. describes recognition of the gp100 proteins by monoclonal antibodies. As argued above, with respect to Maresh et al., gp100 is a distinct gene from

the nucleic acid sequences representing the MART-1 gene and hence cannot anticipate MART-1 sequence. Regarding gp100, Adema et al. describes recognition of the gp100 protein by monoclonal antibodies, but not TIL as required by the instant claim 56. Moreover, Adema et al. does not disclose any gp100 peptides of at least eight contiguous amino acids recognized by TIL. Absent such teaching, Adema et al. cannot anticipate the instantly claimed invention with respect to either gp100 or MART-1.

Kwon et al. describes Pmel-17, which is a gp100 sequence (see specification page 37, lines 6-29). Gp100 or Pmel-17 is a separate and distinct gene from MART-1. Hence, gp100 cannot anticipate the instantly claimed MART-1 sequence. Regarding claim 56 describing nucleic acid sequences encoding at least eight contiguous amino acids recognized by TIL and derived from the gp100 sequence, Kwon et al. does not disclose or describe nucleic acid sequences encoding such peptide sequences. Therefore, neither Kwon et al. nor Adema et al. anticipate the instantly claimed invention. Withdrawal of this ground of rejection is respectfully requested.

REJECTION OF CLAIMS UNDER 35 U.S.C. §103

Claims 56-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO92/21767 in view of Kwon et al. PNAS vol. 88 p. 9228 (1991). Applicants traverse this ground of rejection.

Claims 56-57 are directed to nucleic acid sequences encoding peptides of at least eight contiguous amino acids, which are recognized by TILs, and derived from the

MART-1 or gp100 sequences. PCT Application WO92/21767 discloses that residues 25-53 of gp100 (aka Pmel-17) are recognized by antibodies. However, this reference does not disclose that residues 25-35 of the sequence are recognized by TILs. In fact, the PCT does not disclose any contiguous amino acid sequence of at least eight amino acids recognized by TIL. Kwon et al. describes Pmel-17, but also does not describe any amino acid sequence or portion thereof, that is recognized by TIL, thus Kwon does not remedy the deficiency of the primary reference, and therefore cannot render the claimed invention obvious either alone or in combination. Reconsideration and withdrawal of this rejection is respectfully requested.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for this Amendment, or credit any overpayment to Deposit Account No. 13-4500, Order No. 2026-4124.

In the event that an extension of time is required or which may be required in addition to that requested in the petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or

credit any overpayment for an extension of time to Deposit Account No. 13-4500, Order No. 2026-4124. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

Respectfully submitted,

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Date: March 19, 1997

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